REMARKS

The amendment set forth above adds to the application independent claim 13, as well as several claims that depend from claim 13. New claim 13 is drawn to a method of preventing or treating an NFκB-associated disease or condition in a mammal, in which an NFκB decoy is introduced into the cell. New claim 13 is similar to claim 8 of the parent application, U.S. Serial No. 08/524,206, except that claim 13 is narrower in that it specifies the use of a decoy to a particular transcription factor, NFκB.

Claim 8 was not rejected over prior art in the parent application. Moreover, the operability of the subject matter of claim 13, employing an NFκB decoy, is shown in the enclosed papers. Sawa et al., Circulation 96 (Suppl. II); II-280-II-285, 1997 (a copy is enclosed), for example, describes a study in which NFκB decoys were used to treat ischemic reperfusion injury in the rat myocardium. NFκB decoys were introduced into rat hearts by coronary infusion. Ischemic reperfusion injury in rats that were treated with the NFκB decoys was attenuated as compared to such injury in control rats, which were treated with scrambled decoys. NFκB decoy-treated rats also showed lower levels of neutrophil adherence to endothelial cells and decreased levels of IL-8, as compared to controls, further showing the efficacy of NFκB decoys in treating ischemic reperfusion injury.

In a second paper, Tomita et al., Arthritis & Rheumatism 42(12):2532-2542, 1999 (enclosed), a study is described in which NFκB decoys were used to treat inflammatory arthritis in rats. Briefly, NFκB decoys were introduced into the bilateral hind ankle joints

of rats with collagen-induced arthritis (CIA) by intraarticular injection. This treatment resulted in decreased severity of hind-paw swelling, suppression of joint destruction, and decreased production of IL-1 and TNF-α in the synovium of arthritic joints in NFκB-treated rats, as compared to controls, which were treated with a scrambled oligonucleotide.

Decoys were also shown to have effect in treating inflammation in a paper by D'Acquisto et al., Gene Ther. 7(20):1731-1737, 2000 (enclosed). In this study, local injection of NFκB decoys was shown to reduce inhibit edema formation induced by carrageenin in hind paws of rats.

NFκB decoys were shown to suppress experimental crescentic glomerulonephritis in a third paper, Tomita et al., J. Am Soc. Nephrol. 11(7):1244-1252, 2000 (enclosed). In this study, the decoys were introduced into the left kidneys of rats in which glomerulonephritis had been induced. This treatment resulted in substantial inhibition of disease, as shown by reduced proteinuria, histologic damage, leukocyte infiltration, and cytokine and leukocyte adhesion molecule expression, as compared to scrambled oligonucleotide-treated controls. Similar results were reported by Tomita et al., Gene Ther. 7(15):1326-1332, 2000 (enclosed).

In a paper by Khaled et al., Clin. Immunol. Immunopathol. (2):170-179, 1998 (enclosed), a study is reported in which NFκB decoys were shown to have an effect on immunity. In particular, the decoys were shown to inhibit cytokine production in splenocytes from an autoimmune mouse strain. Decoys were further shown to inhibit

tumor cell growth, *in vitro* and *in vivo*, in a paper by Sharma et al., Anticancer Res. 16(2):589-596, 1996 (enclosed). In particular, this review describes studies that showed that a decoy that is specific for the *RelA* subunit of NFκB blocked tumor cell growth in soft agar, as well as inhibited tumorigenicity in an in vivo tumor model.

The data described in each of the papers discussed above show that NFκB decoys are effective agents in the treatment of NFκB-associated diseases and conditions, as is specified in new claims 13-27.

CONCLUSION

Although no charges are believed to be due, if there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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